Sensory feedback signal derivation from afferent neurons

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QUARTERLY PROGRESS REPORT #10

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I. Summary of the Overall Project

In this study we are exploring the feasibility of extracting 1) cutaneous sensory information about fingertip contact and slip, and 2) proprioceptive sensory information about wrist or finger position. We use implanted nerve cuff electrodes to record peripheral nerve activity in animal models.

Our overall **objectives** for the 3-year duration of this contract are as follows:

1. Investigate, in cadaver material, implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded.
2. Select a suitable animal preparation in which human nerve dimensions and electrode placement sites can be modeled and tested, with eventual human prosthetic applications in mind.
3. Fabricate nerve cuff electrodes suitable for these purposes, and subcontract the fabrication of nerve cuff electrodes of an alternate design.
4. Investigate the extraction of information about contact and slip from chronically recorded nerve activity using these animal models and electrodes. Specifically,
   a. Devise recording, processing and detection methods to detect contact and slip from recorded neural activity in a restrained animal;
   b. Modify these methods as needed to function in an unrestrained animal and in the presence of functional electrical stimulation (FES);
   c. Record activity for at least 6 months and track changes in neural responses over this time.
5. Supply material for histopathological examination from cuffed nerves and contralateral controls, from chronically implanted animals.
6. Investigate the possibility of extracting information about muscle force and limb position from chronically recorded neural activity.
7. Cooperate with other investigators of the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II. Summary of Progress in the Tenth Quarter

During the tenth quarter we undertook various types of analyses of data recorded in the Year Two series of implants. We developed in-house histology techniques for processing samples of instrumented nerves and a brief summary of these techniques and examples of histological data are included in this report. A study of nerve cuff impedance stability over 180 days revealed differences between the suture-type cuffs used in Year One and the baton-type cuffs used in Year Two. We also analyzed EMG contamination of ENG signals recorded while the cats were walking on the treadmill to evaluate our recording devices and protocols. In a collaborative study with Dr. Aleks Kostov, we started to evaluate the quality of ENG and EMG data recorded in the Year Two series during walking and the applicability of machine learning techniques towards processing these signals. We have developed a plan for a series of collaborative studies which are outlined in this report.

We attended two meetings during the quarter, the Canadian Network of Centres of Excellence meeting in Montreal, Canada in May, and the Rehabilitation Engineering Society of North America meeting in Vancouver, Canada in June. An extended abstract was accepted for publication in the proceedings of IEEE SMC 95 in Vancouver, Canada, in Oct., and we submitted an abstract to NeuroScience 95 in San Diego, in Nov.

III. Details of Progress in the Tenth Quarter

A. Summary of Physiological Results from Year Two Implants

Table 1 presents a summary of the Year Two implant series, including total number of days implanted, a description of any problems with implanted nerve cuffs, and changes in nerve compound action potential (CAP) from first to last day. This table was shown in Progress Report #9 and is included again as a reference for later sections of this report. For a full description of the Year Two series please refer to Progress Report #9.

TABLE 1. Year Two data summary as of Feb. 28, 1995

Subject	**Total Days implanted** Final Acute	**Problems with Implanted Cuffs**			**Final Nerve CAP Amplitude**		
		Median	**Ulnar**	**Radial**	**Median** %, last day	**Ulnar** %, last day	**Radial** %, last day
NIH 9	300 FA	prox cuff replaced on day 35 due to nerve injury			100%, 300	76%, 300	
NIH 10	204 FA				108%, 204	117%, 204	
NIH 11	281 FA	large increase in prox cuff impedance after day 180			116%, 180	23%, 281	
NIH 12	289 FA			prox wires broken after day 75	31%, 289		prox wires broken after day 75 106%, 75
NIH 13	180 FA					87%, 180	89%, 180
NIH 14	254 FA			dist wires broken on day 199		130%, 254	70%, 191

B. Histological Procedures

Eight samples from each pair of contralateral control and instrumented nerves were taken from each Year One and Year Two cat in a final acute surgery according to protocols described in Progress Report #4. Samples were processed as follows:

One centimeter long nerve samples were immersed in Karnovsky's fixative, dehydrated and then osmicated for four hours. The osmicated samples were embedded in Jembed 812 (J.B.EM services, Quebec) and then 1 micron sections were cut using a glass knife. The 1 micron sections were counterstained with a 2:1 mixture of Richardson's stain (Richardson, 1960) and Toluidine blue. Sections were examined under a light microscope and colour photographs were taken at various magnifications. The photographs were then scanned to produce electronic images of each processed nerve sample.

C. Initial Histological Findings

Figures 1 and 2 show whole nerve cross sections of the contralateral control and instrumented Ulnar nerves from NIH 13. A preliminary examination of the data indicates several interesting features. The nerve samples from inside the nerve cuffs tend to show both a characteristic increase in the amount of epineurial connective tissue and an increase in the amount of extraneural connective tissue that encapsulates each cuffed sample. These two connective tissue zones are distinctly demonstrated under low magnification (Fig. 1). The corresponding contralateral control samples do not demonstrate this phenomenon (Fig 2).

Figures 3 and 4 show higher magnification views of contralateral control and instrumented Radial nerves from NIH 14. Qualitatively, the axons of a cuffed and a non cuffed nerve are virtually indistinguishable. Axonal shapes and size distributions appear to be similar between the control (Fig. 3) and the experimental (Fig. 4) samples. Quantitative analysis is ongoing at the time of the production of this report.

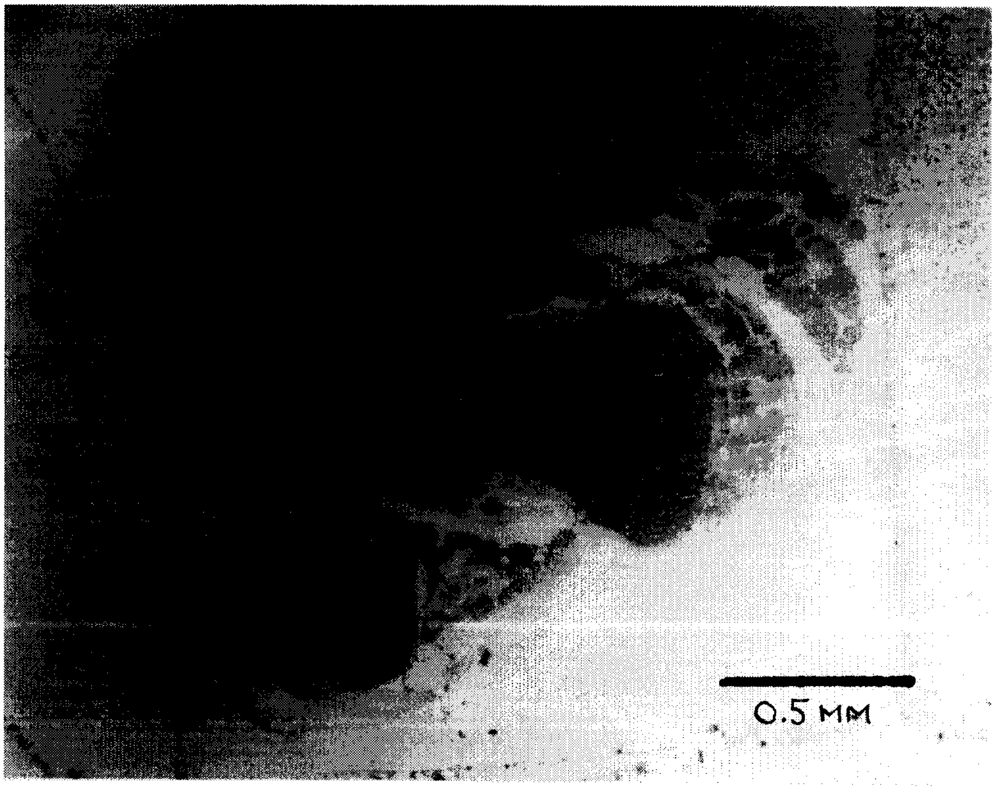

Figure 1: Histology of NIH 13 distal Ulnar nerve control, low magnification (45X)

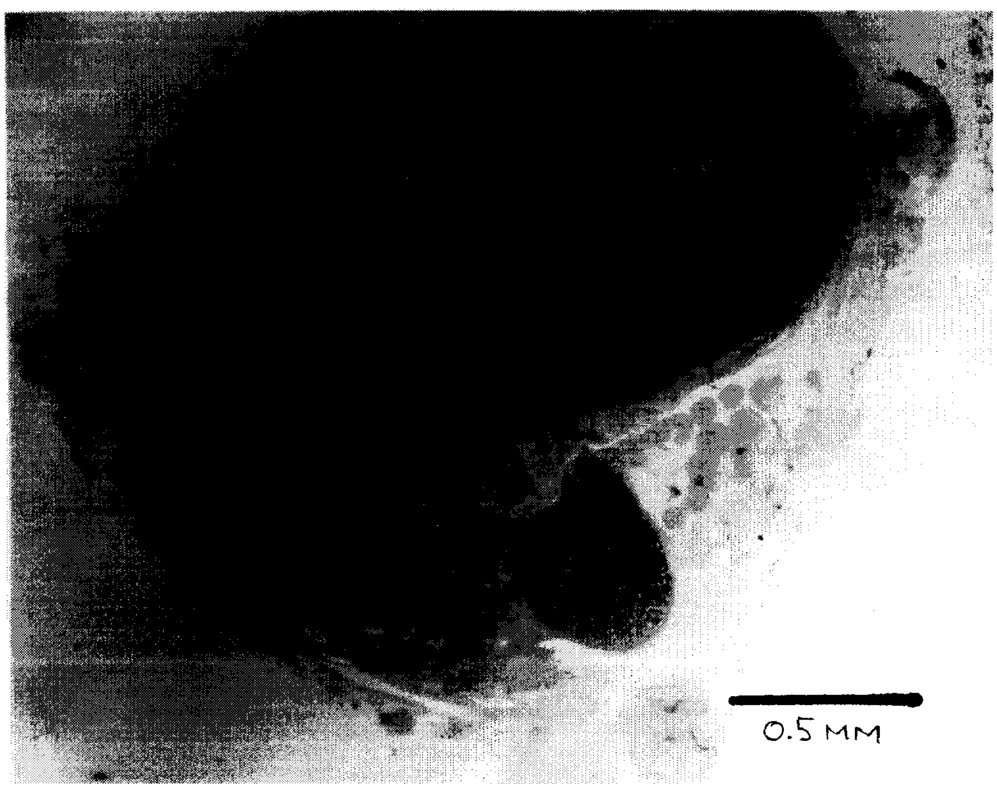

Figure 2: Histology of NIH 13 distal Ulnar nerve experimental, low magnification (45X)

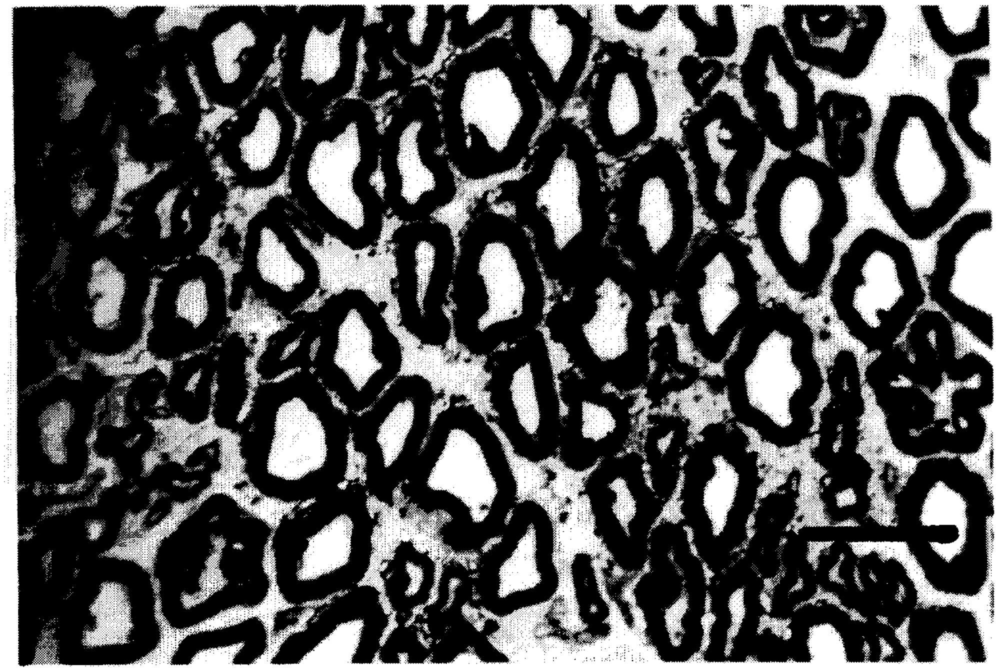

Figure 3: Histology of NIH 14 distal Radial nerve control.
Magnification 800X. Scale Bar is 20 microns.

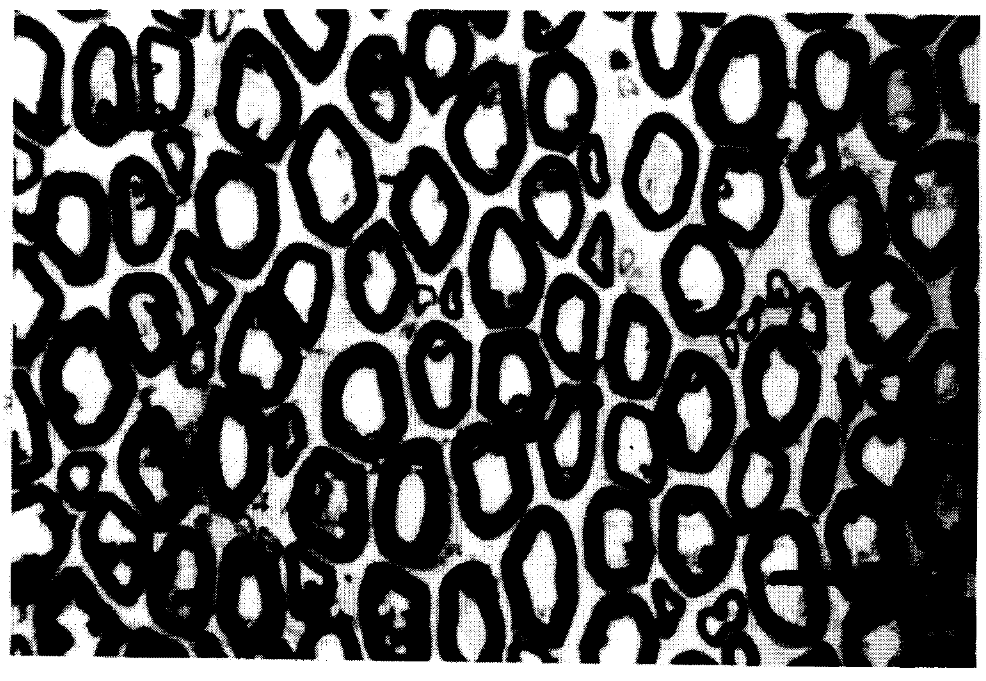

Figure 4: Histology of NIH 13 distal Radial nerve experimental.
Magnification 800X. Scale bar is 20 microns

D. Impedances of Implanted Recording Cuffs

We periodically monitored the cuff impedances during CAP recording session under anaesthesia to evaluate the state of the nerve and the cuff electrodes. We monitored the cuff and EMG electrode impedances (Bak Electronics, Inc. Electrode Impedance Tester model Imp-1) at 1 kHz. Monitoring cuff electrode impedances allowed us to detect and assess problems like pulled wires, cuff seal leakage or electrode breakdown.

Figures 5 and 6 show the geometric means of cuff impedances up to 180 days for both Year One (n=14) and Year Two (n=10) respectively. Only cuffs that had not obviously suffered from pulled wires are included in this analysis. This data set was slightly larger than that for the CAP results reported in PR #9, because we looked at only the distal cuff for impedances, whereas the CAP testing required a functioning distal (recording) and proximal (stimulating) cuff. In NIH 12 the wires to the proximal Radial cuff were broken on day 75 and we could no longer evoke a CAP in the distal cuff, yet we could still monitor the impedance in the distal cuff.

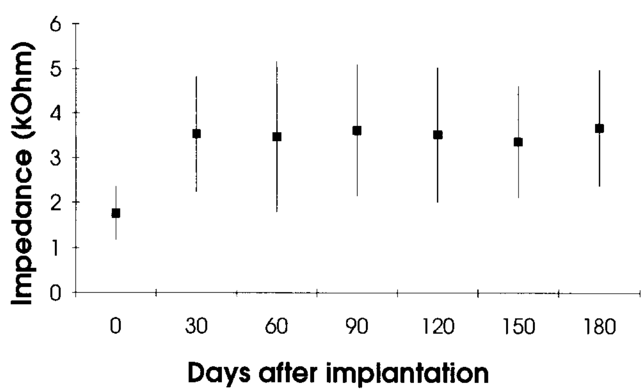

Figure 5: Cuff impedances (±1SD) from Year One (n= 14; cats 2-7) implants

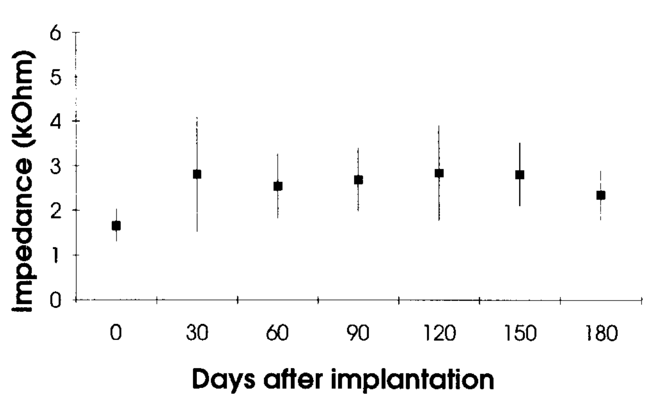

Figure 6: Cuff impedances (±1SD) from Year Two (n = 10; cats 9-14) implants

Both data sets exhibit the characteristic increase in impedance in the first 30 days expected from previous studies (Stein et al., 1978) and then reach a steady-state. The Year Two data show that the new cuff closing technique, consisting of interdigitated closing tubes aligned along the edge of the cuff tubing and a baton inserted through them (as described in PR #4), exhibited lower overall impedances and less variation in the impedances that the suture-type cuffs used in the Year One series.

Reasons for the reduced cuff impedance with the new design are 1) the closing tubes add 0.9 mm to the circumference (approx. 0.3 to the ID) of the cuff which results in a larger cross sectional area and lower impedance, and 2) the outer two reference electrodes were connected togeth~~o~~r at the cuff rather than at the backpack connector, which also reduces the overall cuff impedance. e

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E. Analysis of EMG contamination of cutaneous ENG signals recorded during walking

When recording neural signals a pertinent question is whether the signal is exclusively of neural origin and, if it contains EMG, then how much contamination is present. We performed an analysis of EMG contamination of nerve cuff signals, recorded while the cats were walking at 0.5 m/s on a level treadmill. Thus far we have looked at EMG contamination present in all distal recording cuffs in the first recording session following implantation for each of the six Year Two implants.

The ENG signals were filtered in three stages: 1) highpass filtered (at 65 Hz) by a Leaf Instruments low noise preamplifier (model QT-B5), 2) bandpass filtered (at 500 Hz to 10 kHz) by a Bak Instruments AC differential amplifier (model MDA-1), and 3) highpass filtered (at 1kHz) by an Ithaco filter (model 4302 Dual 24dB/Octave). The filtered nerve signals were displayed on an oscilloscope during recording and were played through a loudspeaker to help ensure that we minimized EMG contamination and recorded mostly ENG signals on FM tape.

The ENG signals were digitally sampled at 20 kHz and then imported into Matlab. The power spectral density was calculated using a 1024 point FFT. The EMG portion of the spectrum was integrated from 0 Hz to 1 kHz and the ENG protion of the spectrum was integrated from 1 kHz to 10 kHz. The ratio of ENG to EMG (signal-to-noise ratio) was calculated and used to evaluate the EMG rejection of the implanted cuffs and the secondary filtering stages. Table 2 below presents a summary of the EMG contamination of Ulnar and Median nerve cuff signals in the cat forelimb.

Table 2: Summary of EMG rejection of nerve cuffs implanted on Ulnar and median nerves implanted in the cat forelimb

Subject	Day	Nerve	ENG/EMG after Bak amplif	ENG/EMG after Ithaco	Increase in ENG/EMG
NIH 9	15	Ulnar	0.04	1.58	38X
NIH 10	29	Ulnar Median	0.20 0.19	9.39 6.35	47X 33X
NIH 11	15	Ulnar Median	0.07 1.35	2.26 42.5	33X 31X
NIH 12	34	Median	0.24	8.89	38X
NIH 13	21	Ulnar	0.07	2.39	36X
NIH 14	14	Ulnar	0.31	6.09	20X
Geometric Mean			0.24	7.99	34X
Standard Deviation			0.43	13.7	7.8X

Table 2 shows that the ENG signals recorded from the Ulnar and Median nerves in the cat forelimb typically show an ENG/EMG SNR of about 8 after highpass filtering at 1 kHz with Ithaco filters. As an example of the spectral densities of the ENG signals, the spectra of the Ulnar nerve ENG recorded from NIH 12 on day 85 are shown in Fig. 7. Figure 7A shows the signal spectrum before Ithaco filtering, and Fig. 7B shows the signal spectrum after Ithaco filtering including a gain of 10 which accounts for the change in amplitude of the ENG peak at approximately 2 kHz. Note that the EMG component (under 1 kHz) of the signal has been reduced and the ENG/EMG SNR is now approximately 10.

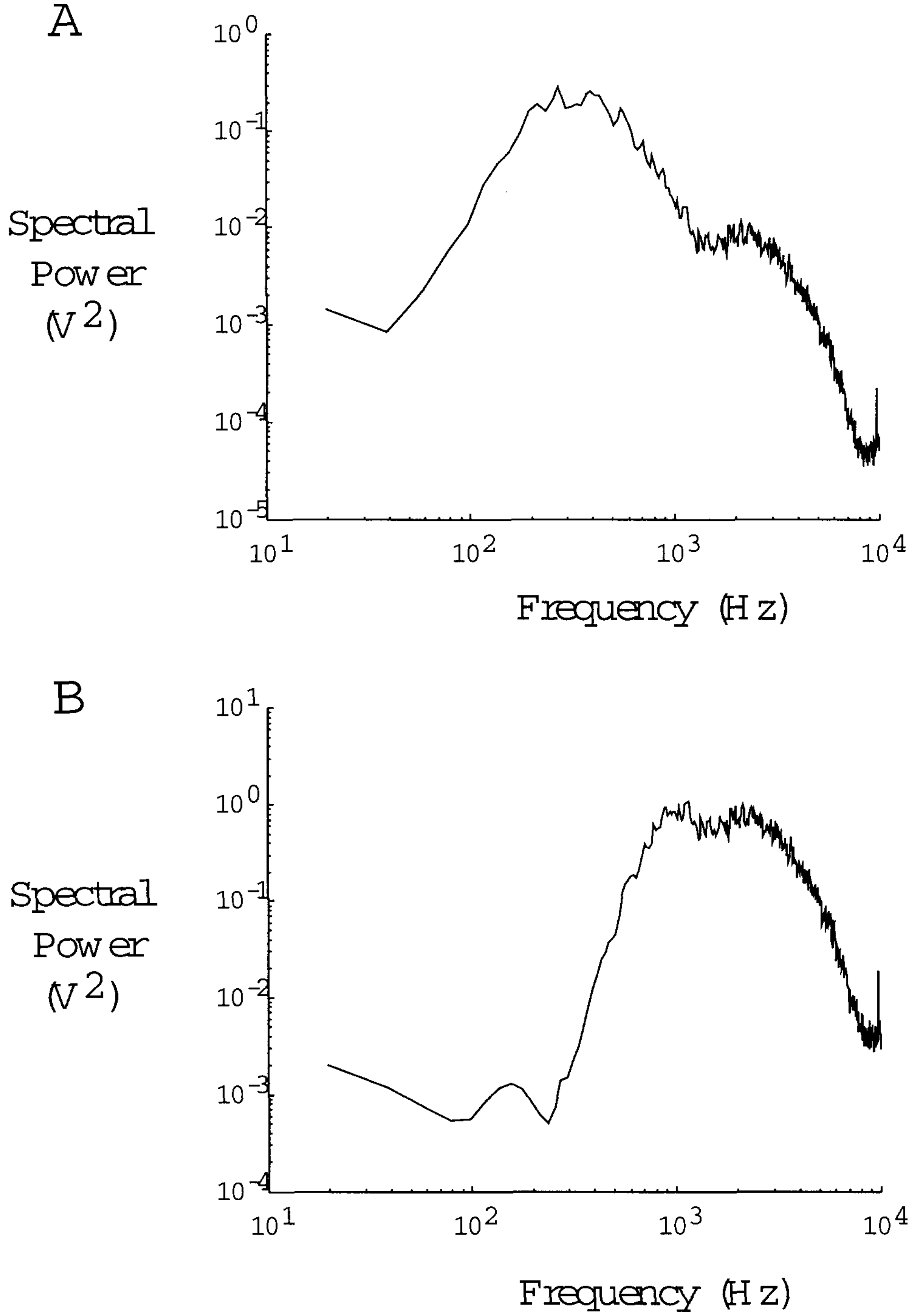

Figure 7: A) Ulnar nerve spectrum before Ithaco filtering,
B) Ulnar nerve spectrum after Ithaco filtering (highpass at 1 kHz, gain = 10)

F. Progress with Collaborators

During the tenth quarter, we made significant progress in a collaborative study with Dr. Aleks Kostov from Edmonton. During a visit to SFU, we developed a systematic approach for determining the feasibility of applying machine learning techniques to analyze cutaneous neural signals and predict muscle activity.

Dr. Kostov has used in his PhD research a machine learning technique (MLT) based on adaptive logic networks (ALNs) to analyze sets of foot contact and pressure signals and predict the activation of a manual switch which a quadriplegic patient used to control stimulation during FES-assisted walking. The ALN was able to learn the pattern of stimulation based on the input signals in a variety of conditions. The system was tested by predicting the stimulation patterns based on new input data and eventually controlling the patterns of stimulation in a demonstration of closed-loop control of FES-assisted walking in the patient.

In our collaborative study we are investigating nerve and muscle data recorded in the cat forelimb during walking on the treadmill. The cutaneous ENG signals are used as inputs to the ALN and the objective is to predict the timing and patterns of EMG signals that are recorded simultaneously as the cat walks on the treadmill. We are investigating the effects of the system parameters on training data by evaluating the error in the predicted signals compared to the actual EMG signals. The next set of studies will be based on testing the generalization of the ALN with test data from the same cat and same recording session as the training data, with test data from the same cat and a different recording session, and finally with test data from different cats. Other variables that will be factored in include the number of ENG signal sources, treadmill speed and treadmill slope.

We expect to demonstrate that MLTs can analyze sets of ENG feedback signals and can accurately predict the required EMG and muscle stimulation patterns to return useful, reliable function to paralyzed extremities. If this approach is proven to be feasible, it may play an important role in the future of FES.

G. Publications and Meetings

During the ninth quarter, an extended abstract authored by Kevin Strange and Andy Hoffer entitled "Using cutaneous neural signals to predict muscle activity during walking in the cat forelimb" has been accepted for publication in the proceedings of the IEEE Systems, Man, and Cybernetics meeting in Vancouver, Canada, Oct. 1995. The paper presents an example of using cutaneous ENG feedback to predict EMG activity in cat forelimb muscles using an off-line state machine controller. A final version of this paper is currently being produced for publication, and a copy will be included in a later progress report.

In addition, Kevin Strange and Andy Hoffer submitted an abstract entitled "Cutaneous neural feedback can be used to predict timing of muscle activation in the cat forelimb during locomotion" for publication in the proceedings of the Neuroscience meeting in San Diego, USA, Nov. 1995.

Andy Hoffer attended the annual meeting of the Canadian Network of Centres of Excellence in Montreal, Canada, in May 1995 and reported current results of this contracted research as well as other related projects in our lab. In addition, Kevin Stange and Paul Christensen attended the Rehabiliation Engineering Society of North America 95 meeting in Vancouver, Canada, and presented the two papers included in Progress Report #9.

IV. Plans for Eleventh Quarter

In the eleventh quarter we intend to:

1. examine histopathologically the nerves from Year One and Year Two cats (objective 5)

3. implant cuffs appropriate for smaller proprioceptive nerves (objective 3)

4. complete the construction of an 8-channel stimulator to be used for FES of forelimb muscles (objective 4b)

5. complete the construction of hardware and begin the software design for controlling the reaching task (objective 4a,b)

6. develop a model of closed loop control of FES during walking utilizing neural feedback (objective 4)

7. analyze walking data with our collaborators (objective 7)

V. References

Stein, R.B., Charles, D., Gordon, T., Hoffer, J.A. and Jhamandas, J. Impedance properties of metal electrodes for chronic recording from mammalian nerves. IEEE Trans. BME 25: 532-537, 1978.